Novel immuno– and stem cell–based therapies
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Abstract — The main areas of the research at the Blood Transfusion Center of Slovenia are cell therapies, stem cells and new diagnostic reagents, based on monoclonal antibodies (mAbs). Our laboratories are equipped for cell-culture work (certified GLP; GMP in reconstruction), molecular biology, immunological techniques and biochemistry. In the course of our research we conducted studies and applied projects (the last mainly industrial) beside production of reagents, with common topic - the antibodies. They were prepared and used to optimise and validate ELISA tests for quality control assessment of the end-product (polyclonal antibodies, in production of drugs), to study protein structure, for immunodiagnostics and as potential immunotherapeutics. Among different mAbs, which we produced in the last decade, a panel of mAbs against prion protein (PrP) and mAbs against bilitranslocase (prepared in collaboration with the University of Trieste) will be studied with different project partners in the scope of Trans2Care. We are fully dedicated to translate the results of the basic research onto applied, possibly clinical level and to contribute to improved healthcare in a sense of advanced modes of immunotherapeutics development and cell based therapies.

Index Terms — human prion protein, prion, bilitranslocase, monoclonal antibodies, immunodiagnostics, immunotherapy, stem cells, cell therapy

1 INTRODUCTION

Blood Transfusion Centre of Slovenia (BTCS) is a national blood bank, responsible for the supply of safe blood and blood components in our country. Beside that, we are providing diagnostic and therapeutic services and blood-derived drugs to our hospitals. We are a strong partner of the University of Ljubljana, giving lectures and providing experimental work to students of graduate studies at Faculty of Medicine,
Faculty of Pharmacy, Faculty of Chemistry and Chemical Technology and Faculty of Health Sciences. We are also involved in postgraduate programs of Biomedicine and Biotechnology at the University of Ljubljana. The same personnel is engaged in research and development at BTCS, being members of three research groups: Tissue Typing Center, Transfusion Medicine and Biomedicine. As of 2004 BTCS has an ISO 9001 standard and is a WHO Collaborating Center and an EFI (European Federation of Immunogenetics) member.

2 RESEARCH AT THE BTCS

Research activities at the BTCS started as early as 1953, when the institution was registered for the research and development in medical biotechnology and medical sciences. In the course of next four decades, activities in this field intensified, especially in the research. During last 15 years the three forementioned research groups, conducted 33 national research projects, 3 national programmes, 6 industrial projects and 6 international projects, financed by Slovene Research Agency, by Ministry for Higher Education, Science and Technology, by industrial partners as well as the European Comission. 18 young researchers/PhD students were trained at the BTCS in the scope of these projects, covering medicine, life sciences and biotechnology. Our development is closely related to our routine operations and services (blood collection and processing, blood grouping, cell therapeutical services) and assures constant education and follow-up in transfusion medicine. The main areas of our research are cell therapies, stem cells and new diagnostic reagents, based on monoclonal antibodies (mAbs). Our laboratories are equipped for cell–culture work (certified GLP; GMP in reconstruction), molecular biology, immunological techniques and biochemistry. On the basis of our research, we were invited to take part of the educational programmes at the University of Ljubljana (see introduction).

2.1 Biomedicine research group

Our research group evolved from the department for the producion of diagnostic reagents, in charge of production of diagnostic reagents for blood grouping under GMP (Good Manufacturing Practice) conditions. Our first research project included the production of potent mouse IgM monoclonal antibodies (mAbs) against ABO blood group system in early nineties of the last century, which were introduced into routine work in the form of diagnostic reagents, registered in 1998. In consequent years, we conducted research and applied projects (the last mainly for the industry) beside production of reagents, with common topic - the antibodies. They were prepared and used to optimise and validate ELISA tests for quality control assessment of the end-product (polyclonal antibodies, in production of drugs), to study protein structure, for diagnostics and as potential therapeutics (mAbs). Among different mAbs, which we produced in the last decade, a panel of mAbs against prion protein (PrP) \[1, 2, 4, 6, 9, 10\] and mAbs against bilitranslocase (prepared in collaboration with the University of Trieste, started in 2006) \[11\] will be studied with different project partners in the scope of Trans2Care.
3 CONTRIBUTION TO TRANS2CARE

3.1 Bilitranslocase

Our current, ongoing collaboration with the T2C partners includes the research of mAbs against bilitranslocase in collaboration with University of Trieste (prof. S. Passamonti). This collaboration will further develop as we anticipate our first joint publications [11].

Figure 1: ICC staining of HepG2 cells with anti-bilitranslocase mAb 6E4/1F2 (40x, 2.4s).

3.2 Prion diseases

In our research on prion diseases we constructed and tested a panel of mAbs against prion protein (PrP) enabling us to distinguish and differentiate between the wild type PrPc and its pathogenic form PrPSc, which is of a great diagnostic value in Creutzfeld Jacob's disease (CJD). This research yielded EU and US patents for these antibodies as well as our common publications with T2C partners SISSA – prof. G. Legname and University of Trieste - prof. R. Gennaro [1, 6]. In the frame of T2C we are aiming at upgrading this collaboration in two possible directions: the use of proteomics for the identification of novel biomarkers of prion diseases using animal models of CJD as well as clinical samples of CJD. These biomarkers could help us elicit the molecular background of prion diseases as well as serve as potential diagnostic or therapeutic tools.

Alternatively we aim at using the expertise and specialized infrastructure (GMP laboratory standards) of the BTCS in the field of cell based therapeutics to research a potential of neural stem cell based therapies for prion diseases using animal models of CJD.
4 CONCLUSIONS

In the frame of T2C, we offer our above mentioned expertise to project partners, within the fields of development of immunotherapeutics, immunodiagnostics, cell based therapies and proteomics as well as wherever sinergies are anticipated. Thus far, we have proven our capacity of inter-regional collaborations and we are looking forward to expanding the ongoing and new collaborations with Slovene and Italian partners. We are fully dedicated to translate the results of the basic research onto applied, possibly clinical level and to contribute to improved healthcare in a sense of advanced modes of immunotherapeutics development and cell based therapies.

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REFERENCES


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